GENOTYPE-PHENOTYPE CORRELATION SHOWS AGE-AT-ONSET-INDEPENDENT EFFECT OF LINGO1 ON ESSENTIAL TREMOR


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Introduction: The marker rs9652490 in intron 3 of LINGO1, a gene important in regulating axon regeneration and oligodendrocyte maturation, has been shown to have genome wide significant association with essential tremor (ET). The role of LINGO1 in the aetiology of ET is largely unknown.

Aims: Genotype-phenotype correlation of the SNP rs9652490 with ET clinical subtypes, including age at onset, presence or absence of family history and head tremor, response to propranolol medication and alcohol, and sex.

Methods: Individuals from the following countries (affecteds/controls): Iceland (230/32811), Germany (225/333), USA (111/387) and Austria (81/241), diagnosed as having ET and having additional clinical subtype information, were genotyped for the SNP rs9652490. ET individuals were divided into 4 groups depending on the age at onset: early onset (0-19y), intermediate onset (20-39y), late onset (40-59y) and very late onset (60y or later).

Results: The ET at-risk variant at rs962490 showed significant association to ET, irrespective of the age at onset. The association was strongest for early and late onset ET (P< 0.001), but also significant for intermediate and very late onset ET (P< 0.05). There was strong association (P< 0.001) irrespective of presence or absence of head tremor, and significant association irrespective of positive or negative response to alcohol (P< 0.001 and P< 0.05, respectively), as well as of family history.

Conclusions: LINGO1 is associated with ET irrespective of age at onset. The association does not vary with presence or absence of family history, head tremor, or positive or negative response to alcohol.